REMARKS

Claims 21, 23 to 25 and 27 to 31 are currently pending in the subject application. Applicants have hereinabove canceled claim 27 without prejudice or disclaimer to applicants' right to pursue the subject matter of this claim in the future. In addition, applicants have amended claims 21, 23, 25, 27, 30 and 31 to recite that the antibody is bound to a cytotoxic agent. Applicants note that the "cytotoxic agent" was previously recited in claim 27, which applicants have cancelled hereinabove without prejudice. Support for the amendments to claim 21 can be found in the specification as originally filed at, *inter alia*, page 62, lines 16-18; page 57, lines 12-14; page 32, line 14 to page 33, line 2; and Fig. 15. Support for the term "cytotoxic agent" in the amendments to claims 23, 25, 27, 30 and 31 can be found at in the specification as originally filed at, *inter alia*, page 62, lines 16-18. Accordingly, applicants maintain that this Amendment raises no issue of new matter and respectfully request entry of this Amendment. After entry of this Amendment, claims 21, 23 to 25 and 28 to 31, as amended herein, will be pending and under examination.

Priority

The Examiner asserted that claims 21, 23-25 and 27-31 are not adequately supported by PCT/US96/02424, of which benefit is claimed. The Examiner asserted that claims 21, 23-25 and 27-31 would be treated as having an effective filing date of January 2, 2004.

In response, applicants first note that the claims as amended hereinabove are drawn to a method of eliminating cancerous prostate epithelial cells comprising contacting

the cells with an antibody bound to a cytotoxic agent, which antibody binds to an outer membrane domain of prostate specific membrane antigen having the sequence set forth in SEQ ID NO:128.

Applicants note that support for such a method can be found in the specification as originally filed (and in PCT/US96/02424), for example, at page 32, lines 23 to page 33, line 2, which discloses selecting hydrophilic amino acid sequences to generate antibodies. In addition, page 32, lines 14 to 17 of the specification as originally filed (and PCT/US96/02424) recite that "with the protein sequence information, antigenic areas may be identified and *antibodies directed against these areas may be generated and targeted to the prostate cancer* for imaging the cancer *or therapies.*" (Emphasis added). Moreover, the specification as originally filed (and PCT/US96/02424) state that the "antigen has the characteristics of a membrane spanning protein with the *majority of the protein on the exofacial surface*" at page 60, lines 18-21. (Emphasis added). Furthermore, the specification (and PCT/US96/02424) state at page 62, lines 16-18 "[a]ntibodies against PSM antigen *coupled with a cytotoxic agent will be useful to eliminate prostate cancer cells*". (Emphasis added). Thus, there is support for the claimed method including support for providing antibodies that bind to PSMA, the outer membrane domain, support for use of those antibodies in therapies, and for the elimination of prostate cancer cells by antibodies coupled to a cytotoxic agent. Accordingly, applicant maintains that support for the claimed method is found in the specification, and in PCT/US96/02424 of which benefit is claimed.

Claims rejected under 35 U.S.C. §112 (Second Paragraph)

The Examiner rejected claims 21, 23-25 and 27-31 under 35 U.S.C. §112, second paragraph, as allegedly indefinite as to "how the antibody is bound to a substance effective to kill, ablate or eliminate cells." The Examiner also asserted that if "ADCC" is involved in the claimed invention it is not clear why normal cells are also eliminated. The Examiner further stated that the "substance" as recited in the phrase "substance effective to kill" is not clear.

In response, applicants respectfully traverse the Examiner's rejection.

However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicants have herein amended claim 27, from which the remaining rejected claims depend, to recite that the cells are contacted with an antibody bound to a cytotoxic agent under conditions effective to permit both binding of the antibody to the outer membrane domain of the prostate specific membrane antigen and eliminating said cells. Accordingly, applicants maintain that the claims as amended hereinabove are definite and clear and therefore respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Claims rejected under 35 U.S.C. §112 (First Paragraph, Written Description)

The Examiner rejected claims 21 and 23-25 as failing to comply with the written description requirement as drawn to new matter. The Examiner asserted that although the

instant specification provides and teaches "that antibodies against PSM coupled with a cytotoxic agent will be useful to eliminate prostate cancer cells (page 68, line[s] 16-24) [it] does not provide sufficient support for the instant claims reciting eliminating prostate cancer cell[s] or epithelial cells by an antibody only" (Examiner's emphasis). The Examiner also asserted that the specification does not provide a method of eliminating a normal, BPH or prostate cancer epithelial cells by an antibody binding "to the outer membrane of prostate cancer cells."

In response, applicants respectfully traverse the Examiner's rejection.

However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicants have herein amended claim 27, from which the remaining rejected claims depend, to recite that the cells are contacted with an antibody bound to a cytotoxic agent under conditions effective to permit both binding of the antibody to the outer membrane domain of the prostate specific membrane antigen and eliminating said cells. As applicants have noted hereinabove, the specification provides support for such a therapy. For example, the specification (and PCT/US96/02424) state at page 62, lines 16-18 "[a]ntibodies against PSM antigen coupled with a cytotoxic agent will be useful to eliminate prostate cancer cells". Accordingly, applicants maintain that the claims as pending are sufficiently described in the specification as filed, and as such raise no issue of new matter.

The Examiner also rejected claims 21, 23-25 and 27-31 under 35 U.S.C. §112, written description, asserting that the specification on pages 244-245 teaches a computer-predicted membrane-spanning domain of PSMA and states that this data enables prediction of inner and outer membrane domains which aids in designing antibodies for use in targeting and imaging prostate cancer. The Examiner asserted that the specification does not disclose any such antibodies, nor any method using such an antibody, to kill or eliminate cells of the prostate due to binding of the antibody to an outer membrane domain of PSMA. The Examiner further stated that the application does no more than describe the desired function of the claimed antibodies. The Examiner also stated that "[w]ithout possession of the antibodies (that [are] specific to the outer membrane domain), the claimed endpoints are illusory and there is no meaningful possession of the method."

In response, applicants respectfully traverse the Examiner's rejection.

Applicants note that according to MPEP §2163 "disclosure of an antigen fully characterized by its *structure*, formula, chemical name, physical properties, or deposit in a public depository *provides an adequate written description of an antibody claimed by its binding affinity to that antigen*. Noelle v. Lederman, 355 F.3d 1343, 1349, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (emphasis added). Applicants further note that claim 27, as amended, recites that the antibody provided in the claimed method "binds to an outer membrane domain of prostate specific membrane antigen having the sequence set forth in SEQ ID NO:128". Applicants therefore

maintain that it is clear that the recited antibodies are adequately described. In addition, the specification specifically discusses using such antibodies coupled with a cytotoxic agent to eliminate prostate cancer epithelial cells. Accordingly, applicants maintain that the method as claimed, including the antibody recited in the method as claimed, are adequately described by the specification.

Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Claims rejected under 35 U.S.C. §103(a)

The Examiner rejected claims 21, 23-25 and 30-31 under 35 U.S.C. §103(a) over Murphy et al. (Prostate, 28:266-271, 1996) in view of Horoszewicz et al. (Anticancer Research, 7:927-935, 1987) and Horoszewicz et al. (U.S. Patent No. 5,162,504, issued 1992).

In response, applicants respectfully traverse the Examiner's rejection. Applicants note that the primary reference relied upon by the Examiner, Murphy et al., was published in April of 1996, i.e. after the filing date of PCT/US96/02424 (February 23, 1996). In addition, applicants have noted hereinabove how the claims as amended hereinabove are supported by the priority document PCT/US96/02424. As such, Murphy et al. is *not* prior art to the claims pending in the subject application. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

If a telephone conference would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the total enclosed fee of $930.00, including a $405.00 Request for Continued Examination ("RCE") fee and a $525.00 fee for a three-month extension of time, is deemed necessary in connection with the filing of this Amendment and RCE. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:
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